

## PATENT ABSTRACTS OF JAPAN

(11)Publication number : 2004-002271

(43)Date of publication of application : 08.01.2004

(51)Int.Cl.

A61K 9/08  
A61J 1/10  
A61K 38/48  
A61K 45/00  
A61K 47/10  
A61P 7/04  
B65D 21/08

(21)Application number : 2002-287208

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(22)Date of filing : 30.09.2002

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(30)Priority

Priority number : 2001338762  
2002081984Priority date : 29.09.2001  
22.03.2002Priority country : JP  
JP

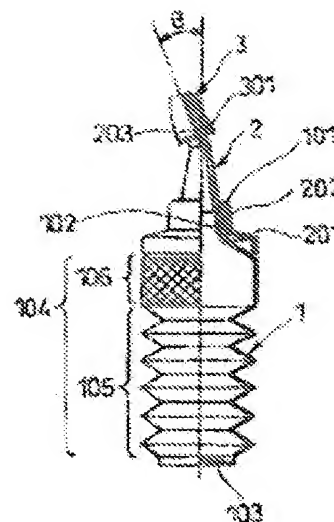
## (54) TOPICAL STYPTIC MEDICINE COMPOSITION SEALED IN FLEXIBLE CONTAINER

(57)Abstract:

PROBLEM TO BE SOLVED: To impart discriminability from other liquid agents in operation processes, and to avoid the occurrence of an immediately injectable form.

SOLUTION: This topical styptic medicine composition sealed in a flexible container to administer the composition on an endoscopic treatment or the like. The flexible container is composed of a flexible container body 1, a nozzle-having cap 2 mounted on the mouth portion 101 of the main body, and a nozzle cap 3. The bellows portion 105 of the container body 1 is pressed and compressed with fingers to jet the medicine liquid in the container into a washing tube or the like.

Consequently, a medical treatment error based on an injection misuse liable to be caused on the administration of a conventional topical styptic medicine composition can be prevented.



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CLAIMS

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[Claim(s)]

[Claim 1]

A medicinal composition for partial hemostasis sealed hermetically in a flexible container.

[Claim 2]

The medicinal composition for partial hemostasis according to claim 1 sealed hermetically in a flexible container since a medicine was prescribed for the patient at the time of endoscope treatment.

[Claim 3]

Claim 1 or a medicinal composition for partial hemostasis given in two which is what has at least two or more features of the following [ container / flexible ].

1) A flexible part is a product made from a plastic.

2) Include bellows (BEROSU) structure to a flexible part.

3) A portion between package body regio-oralis male screw Motobe of a flexible container and a bellows portion is the shape of dome state or conical shape.

4) It is disengageable to a cap with a nozzle, and a flexible package body at least before contents enclosure.

5) A nozzle equips 10 degrees of ascending vertical angles thru/or 90 degrees with structure which crooked or curved from a container medial axis.

6) A nozzle tip can be opened for free passage with foam-connection gold of an endoscope forceps opening or a washing tube for nebulization and spraying.

[Claim 4]

A medicinal composition for partial hemostasis of Claims 1-3 containing thrombin as an active principle at least given in any 1 paragraph.

[Claim 5]

A medicinal composition for partial hemostasis of Claim 4 by which 40 to 55% (W/V) of glycerin being included during a presentation.

[Claim 6]

A flexible container for enclosing a medicinal composition for partial hemostasis which has following at least two or more features.

1) A flexible part is a product made from a plastic.

2) Include bellows (BEROSU) structure to a flexible part.

3) A portion between package body regio-oralis male screw Motobe of a flexible container and a bellows portion is the shape of dome state or conical shape.

4) It is disengageable to a cap with a nozzle, and a flexible package body at least before contents enclosure.

5) A nozzle equips 10 degrees of ascending vertical angles thru/or 90 degrees with structure which crooked or curved from a container medial axis.

6) A nozzle tip can be opened for free passage with foam-connection gold of an endoscope forceps opening or a washing tube for nebulization and spraying.

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DETAILED DESCRIPTION

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[Detailed Description of the Invention]

[0001]

[Field of the Invention]

This invention is a medicinal composition for the partial hemostasis containing a flexible container. In order to aim at prevention of the malpractice which tends to happen in detail at the time of administration of the medicinal composition for partial hemostasis, and the malpractice at the time of a medicine especially being prescribed for the patient at the time of endoscope treatment, it is related with the medicinal composition for partial hemostasis sealed hermetically especially in the flexible container, and is used in a medical field.

[0002]

[Description of the Prior Art]

In an upper gastrointestinal tract etc., when bleeding which oozes from an ulcer etc. is accepted by endoscopy, it is common to spray or irrigate a bleeding part with the hemostat for parts from the tip of an endoscope, and to stop bleeding. As a hemostat used for these purposes, vasoconstrictors, such as an epinephrine injection, sodium alginate, thrombin, etc. are raised. In those pharmaceutical preparation, thrombin liquids and solutions are conventionally enclosed with the vial bottle.

As an example of the thrombin liquids and solutions enclosed with the vial bottle, patent-documents 1 grade is mentioned, for example, and it is indicated as a constituent for partial hemostasis which blended the coloring matter for malpractice prevention.

[0003]

[Patent documents 1]

JP,2002-104996,A

[0004]

[Problem(s) to be Solved by the Invention]

In the pharmaceutical preparation for hemostasis, the maker is displaying "\*\*\*\*\*", "it being \*\*\*\* about injection", etc. on a package, a vial, etc. uniquely until now so that the drugs for the local administration containing a vial bottle may be seen by the liquids and solutions for parts of thrombin, for example. However, also to the pharmaceutical preparation for hemostasis by one side like plasmin antagonists, such as tranexamic acid, or ethamsylate, There is a drug solution in which the whole body administration, or the hypodermic and intramuscular injection by an intravenous injection is accepted, From the belief with "vials are injections", the drugs which are originally the objects for local administration were accidentally injected in the blood vessel, the accident in which a patient dies has occurred, and the policy of the radical prevention from misuse was called for from the side of malpractice prevention.

[0005]

In [ generally, the pharmaceutical preparation containing a vial bottle attracts and extracts a drug solution in a glass syringe with a glass syringe with a hypodermic needle at the time of use, and ] a partial hemostat, A hypodermic needle is demounted after that and the method of connecting with foam-connection gold of the washing tube for nebulization and spraying equipped with the nozzle of the glass syringe by the endoscope forceps opening and the

endoscope, and prescribing a drug solution for the patient is taken. For this reason, operation of the medical site was complicated, and although a possibility of becoming a cause which attracts a malpractice was pointed out, this invention persons were taken as the radical issue which should solve distinctive grant with other liquids and solutions in an operation process, and the occurrence avoidance of the gestalt which can be injected instantly.

[0006]

Furthermore, the drugs containing a vial bottle separated the glass bottle, the rubber stopper, and the cap made from aluminum (eye plastic cap + aluminum winding up) after use, further, separate disposal also of a hypodermic needle and the glass syringe had to be carried out, it is very troublesome, and an improvement was desired.

[0007]

Although the granule preparation of the separate-packaging gestalt was also developed about thrombin preparation, the pharmaceutical preparation concerned is put into a container suitable at the time of use, and after dissolving with suitable solvents, such as a phosphate buffer solution, it is necessary to use it. Therefore, in the correspondence in an emergency in bleeding, etc., the thrombin preparation of the gestalt which is easier to use it was called for.

[0008]

[Means for Solving the Problem]

Artificers of this invention by providing a medicinal composition for partial hemostasis beforehand sealed hermetically in the completely different below-mentioned flexible container from a vial container, It found out that the operativity of a medical site could be raised, and discernment from shape could be made easy, and a process using a glass syringe (glass syringe with which it was especially equipped with a hypodermic needle) could be removed from an operation process, above-mentioned SUBJECT of reducing a malpractice was solved, and this invention was completed.

[0009]

[Embodiment of the Invention]

The mode of operation of this invention is explained below.

Mode 1

[1-1] This invention is the medicinal composition for partial hemostasis sealed hermetically in the flexible container. Here, a flexible container is a container which gave the function for making contents start that it is running by having a flexible part which consists of flexible construction material and structure in some or all of containers, changing and pressing and shrinking the flexible part concerned.

[1-2] Since a medicine is especially prescribed for the patient at the time of endoscope treatment, it is a medicinal composition for partial hemostasis of the mode 1-1 sealed hermetically in the flexible container. The constituent concerned is usually a fluid at a room temperature.

[0010]

[1-3] A flexible container is the mode 1-1 which has following at least two or more features of 1-6, or a medicinal composition for partial hemostasis of 1-2.

- 1) A flexible part is a product made from a plastic.
- 2) Include bellows (BEROSU) structure to a flexible part.
- 3) The portion between package body region-oralis male screw Motobe of a flexible container and a bellows portion is the shape of dome state or conical shape.
- 4) It is disengageable to the cap with a nozzle, and a flexible package body at least before contents enclosure.
- 5) A nozzle equips 10 degrees of ascending vertical angles thru/or 90 degrees with the structure which crooked or curved from a container medial axis.
- 6) A nozzle tip can be opened for free passage with foam-connection gold of an endoscope forceps opening or the washing tube for nebulization and spraying.

In the medicinal composition for partial hemostasis sealed hermetically in this container, a suitable vasoconstrictor, sodium alginate, thrombin, etc. can be used as an active principle.

[0011]

[1-4] It is the mode 1-1 thru/or the medicinal composition for partial hemostasis of 1-3 description containing thrombin as an active principle especially at least.

After especially thrombin liquids and solutions filtrate aseptically the thrombin liquids and solutions prepared by agitating and equalizing after adding a stabilizing agent and buffers, such as polyol, to the thrombin obtained by the conventional method and mixing to it, a flexible container is filled up with them and a medical institution is provided with them. In a medical institution, it passes, and endoscopic or it is used by taking orally etc. to the bleeding part of a part.

[0012]

[1-5] It is a medicinal composition for partial hemostasis of the mode 1-4 furthermore characterized by including 40 to 55% (W/V: weight/capacity) of glycerin during a presentation. As a constituent for partial hemostasis of this invention, as for the liquids and solutions of thrombin used typically, 40 to 55% (W/V) of polyol division glycerin is usually more preferably used 10 to 60% (W/V) as a stabilizing agent. If there is much quantity of glycerin, since viscosity will become high, there is fault -- sufficient diffusion is not obtained, even if the press by one hand becomes difficult or it presses, when sprinkling to a bleeding part via an endoscope or a washing tube. In order to be able to carry out the long term storage of the thrombin in solution states, it is required to add a constant rate of glycerin, but in this invention, it is preferred to make glycerin more than 40% (W/V) contain below at 55% (W/V).

[0013]

## Mode 2

The flexible container used for this invention is explained in full detail below.

[2-1] In the flexible container used for enclosure of the medicinal composition for partial hemostasis of this invention with a flexible container. It is the container which gave the function for making contents start that it is running by having a flexible part which consists of flexible construction material and structure in some or all of containers, changing and pressing and shrinking the flexible part concerned. Preferably, it is a container of the features 1-6 indicated below for which it has two [ or more ] or more all [ three ] still more preferably more preferably. As shape of a container, although various shape, such as a sphere and a barrel, can be taken, the cylinder-like-object-with-base-like object which has an opening may usually be preferred, and any of the cylinder body of suitable length and an rectangular pipe object may be sufficient as a tube-like object. The sectional shape of an rectangular pipe object may be a polygon of an octagon object besides a triangle, a quadrangle, and a hexagon etc.

[0014]

[2-2]

Feature 1: A flexible part is a product made from a plastic.

The construction material of a flexible part is not limited especially unless a problem is produced in the stability of drugs and adsorption which are the raw materials which bring about flexibility and are originally enclosed. For example, it may be formed from elastomers, such as crude rubber and synthetic natural rubber besides plastic resin. In order to give fixed shape preferably, the thing made from a plastic is desirable.

In this invention, as a plastic which constitutes a flexible package body, As long as it has elasticity and flexibility, there is no restriction in particular and may choose from the thermoplastics mentioned later, and its mixture and layered product suitably, but. Especially polyolefin system resin, such as polyethylene and polypropylene, is preferred at the point which the safety of excelling in the moldability and the use to a medical field has established.

[0015]

Although it can choose from the wide range suitably regardless of whether polyethylene is high-density or it is low density, low density polyethylene is suitable for the flexible part of a package body, considering the viewpoint of pliability or transparency. As polypropylene, a copolymer with a small amount of (generally 10 or less % of the weight, preferably 5 or less % of the weight) olefins, such as a homopolymer or ethylene, and 1-butene, is available, and the thing of the grade currently used widely as a medical container is suitable.

[0016]

[2-3]



Feature 2: Include bellows (BEROSU) structure to a flexible part.

The package body is equipped with the flexible function as a flexible part, and if it is applying power, and changing or shrinking a flexible part from the exterior and is the shape which can discharge an inner solution smoothly, shape in particular will not be limited. For example, a balloon with the thing which consists of a simple infusion solution bag, or elasticity can also be used.

[0017]

If the utilizing method used as the hemostat for parts and the operativity which it divides and passes and is by one hand in the case of endoscopic administration are taken into consideration, When the size settled in the palm of one hand as a size of a container applies predetermined \*\* to a flexible part preferably, it is desirable to have the first fixed shape for contraction to occur, especially bellows shape.

Although the shape in particular of bellows is not specified, what gave the \*\* rose indicated by the shape of the bellows whose gap is almost lost in a package body at the time of press contraction, for example, JP,62-180445,U, JP,6-3349,U, etc. is mentioned so that a drug solution besides simple bellows may fully start that it is running. The path of bellows can also be set up become little by little small toward a bellows pars basilaris ossis occipitalis (fingerplate pressing part).

Although the number in particular of bellows is not specified, it is possible to set up suitably by the operativity at the time of press contraction, the ejection nature of a drug solution, the ease of carrying out of manufacture, etc. It is preferred that they are about 3-10 steps.

For example towards the opening of a package body, a bellows portion is provided so that compression is possible, but a bellows portion may be formed so that it may be in the state which it does not restore after press / compression, i.e., is compressed, or it may be formed with such construction material including a package body. For example, it forms with a rigid plastic, it divides into every lot (or one belly), two steps, or three-stage of bellows, and may enable it to compress.

[0018]

Or even if it is a case where a gap remains in a container, can fully eject a drug solution from the container which turned the nozzle downward by enclosing beforehand the gas (inactive gas disinfected preferably, such as air and nitrogen gas) of sufficient quantity to replace a gap with a drug solution, but. At this time, the content volume of a container needs to balance it.

In this invention, it is desirable to eject a drug solution as much as possible also from \*\*\*\* of an endoscope or a washing tube, and, in this case, it is especially good to include the content volume of the \*\*\*\* concerned further and to set up the content volume of a flexible container.

[0019]

The quantity of the drug solution prescribed for the patient with the flexible container of this invention is about 5 ml - 20 ml. The final gaps after compression of the flexible container which has bellows are usually 5 ml - 30 ml. The content volume of a washing tube etc. is usually 3 ml - about 5 ml. Therefore, about 10 ml - 50 ml of content volume of the flexible container of this invention is preferably set to 20 ml - 40 ml.

[2-4]

Feature 3: The portion between package body regio-oralis male screw Motobe of a flexible container and a bellows portion is the shape of curvature shape or conical shape.

The shape applied to a package body regio-oralis male screw part from a bellows portion, That which is horned in the length direction (shaft orientations) sectional shape of a container so that it may be cylindrical (anchor shoulder shape), Like conical shape, although the things of curvature shape (sloping-shoulders shape), etc. may be any like a linear thing and the shape of dome (dome), it is desirable that it is the shape where a drug solution does not remain in a container as much as possible. For this reason, it is preferred that the section which does not have an angle like shape with a linear section or dome state like the truncated cone shape which an apex carries out an opening and touches the package body regio oralis gives the shape (sloping-shoulders shape) of curvature shape. If such shape has such the shape of the inner skin of a container at least, it is good.

[0020]

[2-5]

Feature 4: It is disengageable to the cap with a nozzle, and a flexible package body at least before contents enclosure.

Integral moulding of the flexible container may be carried out from the nozzle for the same raw material even to the package body. In this case, the copolymers of the thermoplastics to which the thickness can be changed according to desired flexibility (or rigidity), for example, polypropylene, polyethylene, polystyrene and propylene, ethylene, and/or styrene can be enumerated. In addition, polyvinyl chloride, an ethylene-vinylacetate copolymer, polyamide, Polyvinylidene chloride, polyvinyl fluoride, poly trifluorochloroethylene, polyethylene terephthalate, polyester, polyolefin system resin, and these mixtures and layered products are also mentioned. In the case of integral moulding, it is also still more possible to perform simultaneously shaping of a drug solution seat part, restoration of a drug solution, and attachment of the nozzle for drug solution regurgitation with an automatic blow restoration seal molding method.

From the facilities of the drug solution restoration used widely, a package body and the cap with a nozzle are fabricated independently, and what can combine both is preferred by fitting or screw lump before restoration of a drug solution etc., or to the back.

It is also possible by attaching about ten screw return prevention projections to the package body regio-oralis lower part of a flexible container, for example, and providing about four screw return prevention ribs in the female screw lower part of the cap with a nozzle further, for example to have a mechanism which prevents the slack of a screw.

[0021]

Especially, when a container is held single hand, a thumb portion is assigned to the pars basilaris ossis occipitalis (fingerplate pressing part) of the bellows of a flexible part division package body. When the portion (fingerplate part) which can hold a container certainly with other fingers exists and both are used for the cap side with a nozzle as one, it is desirable to become the structure which can apply sufficient power for compression from the exterior only single hand, and is made to discharge content fluid. Usually, although it is made for the size of this pars basilaris ossis occipitalis to become a slightly smaller diameter compared with a bellows portion, what is necessary is just a thing of the diameter which restriction in particular will not have if sufficient power for compression can be applied, and can be pushed in a thumb portion. When it holds single hand, compressing is also possible, as a palm is assigned to a pars basilaris ossis occipitalis, an index finger and the middle finger are applied to the fingerplate part of the cap with a nozzle, for example and the whole container is wrapped in.

The structure (for example, rib) for giving the suitable intensity for a cap to the back side of the cap with a nozzle may be provided in two or more places. The outside surface shape applied to a package body regio-oralis male screw part from a bellows portion although there is no restriction in particular the shape of this rib. When it is that (anchor shoulder shape) horned, a thing of the curvature shape (sloping-shoulders shape) which does not have an angle like a linear thing or dome state like conical shape, etc. in the sectional shape of a package body so that it may be cylindrical, it may be set up suitably correspond to these shape.

Finger charge's projection or hollow which can recognize the bending direction of a nozzle may be established in the fingerplate part of the cap with a nozzle. If this projection or hollow is the shape which can recognize the bending direction of a nozzle, there will be no restriction in particular. For example, the projection of thin length is mentioned.

[0022]

Although the raw material of a nozzle may be the same as a flexible package body as mentioned above, in order to be fixed to a washing tube or an endoscope forceps opening at the time of a free passage. It is preferred to use the rigid plastic represented by high-density polyethylene and polypropylene, ABS plastics, polycarbonate, etc. in order to have sufficient rigidity.

[0023]

[2-6]

Feature 5: A nozzle equips 10 degrees of ascending vertical angles thru/or 90 degrees with the



structure which crooked or curved from the medial axis, when a container is a barrel.

Although the shape in particular of the nozzle part at the tip which content fluid discharges is not limited, either, the shape which holds a container at the angle that operation of compression of a flexible container, etc. is made easy as much as possible at the time of an endoscope or a washing tube free passage, and a drug solution does not remain the drugs for partial hemostasis as much as possible in a bellows portion is desirable. For this reason, about the jet direction of a nozzle, what gave the predetermined ascending vertical angle from the axis of the container is preferred.

Therefore, the nozzle of this invention equips 10 degrees of ascending vertical angles thru/or 90 degrees with the structure which crooked or curved from a container medial axis preferably.

They are 10 degrees - 40 degrees of ascending vertical angles more preferably. Crookedness or a curve may be a specific place from the base to a tip of the whole nozzle or a nozzle. A nozzle is especially crooked into the character of "\*\*" by 10 degrees - 20 degrees of ascending vertical angles preferably.

[0024]

[2~7]

Feature 6: A nozzle tip can be opened for free passage with foam-connection gold of an endoscope forceps opening or the washing tube for nebulization and spraying.

In order to present the treatment of an endoscope etc. with these drugs, without filling up a glass syringe with a drug solution again, they need to pour the filled drug solution into an endoscope etc. directly from a container. For this reason, it is required for a flexible container and foam-connection gold (foam-connection part) of an endoscope forceps opening or the washing tube for nebulization and spraying to be able to be open for free passage via auxiliary tools, such as direct or suitable length, a tube of shape, and an applicator. Therefore, what is the size and shape which the nozzle of a flexible container can connect to foam-connection gold of a direct endoscope forceps opening or the washing tube for nebulization and spraying is preferably good.

[0025]

In addition, multiple times may be divided and medicated when prescribing a topical styptic for the patient using this flexible container. In order to prevent fault, such as sucking in the blood from the affected part, etc. especially at this time, a check valve (feature 7) may be further provided in the inside of a nozzle tip or a nozzle. The valve of the chemical-feeding machine of a description, etc. are referred to as a suitable example at JP,S62-180445,U and JP,S59-85236,U. The cap (it is hereafter described as a nozzle cap) for enclosing a drug solution and if needed, after being filled up with a gas is attached to a nozzle. At this time, a nozzle cap made from a suitable elastomer can be used, and also the gestalt (feature 8) which can screw the nozzle cap made from a plastic in which the male screw was given to the nozzle periphery and the female screw was given is preferred.

The part (feature 9) for sticking suitably labels about discernment of a drug or handling, such as "muscle injection" and "being \*\*\*\* about injection", can be established in the container concerned. By pasting of this label, it differs from the conventional mere glass syringe, and just before administration or during administration, the drug concerned can be recognized and attention can be paid.

If needed, by making the flexibility of this pasting part high, at the time of use, crush a pasting part together with a bellows portion, or. Conversely, a pasting part is likened with a coat pipe, rigidity may be made high and also the device which pushes in a bellows portion in a pasting part and keeps it compactly may be performed after drug solution discharge. When the shape of the cap with a nozzle is the shape which attaches a furnace to the lower part of the fingerplate part to a bellows portion, it is possible to make the \*\*\*\*\* surface into the part for sticking a label. When making the \*\*\*\*\* surface into a label attachment part, it replaces with a label and is directly good as for printing or a protrusion in a cautions character.

[0026]

The pouring device (feature 10) which has a flexible part for a coat pipe, pistons, etc., such as a wrap cylinder, may be used for compression of a container. That is, it is also possible to cover a

flexible part with a coat pipe and to use it at a piston etc., pushing the pars basilaris ossis occipitalis of a container. Such a coat pipe may be united with the flexible container, or may be an attachment-and-detachment type. In the case of an attachment-and-detachment type, although the nozzle of a container fully comes out of one end of a coat pipe out of a pipe, the container itself is constituted so that it may press at the piston which shall have a suitable omission preventive mechanism and was inserted from the end of another side so that it might not fall out. The coat pipe with which the hole a little smaller than the diameter of a flexible container section was suitably formed in the cylindrical end is preferred.

The coat pipe concerned may be equipped with the window of the suitable size which cut and lacked a part of periphery of the pipe in order to carry out attachment and detachment of a flexible container easily to others. The window concerned may be a thing of sliding types, such as the unvented system or hinge represented by the mere OFF Li \*\*\*\* part, and with a slide door.

[0027]

[2-8]

Each of the above features 7~10 is suitably combined with two or more features of the features 1~6, and can constitute the feature of the container of this invention.

For example, when said feature 10 is combined, the flexible container used for enclosure of the medicinal composition for partial hemostasis of this invention is a container for enclosing the medicinal composition for partial hemostasis which has following at least two or more features indicated below.

- 1) A flexible part is a product made from a plastic.
- 2) Include bellows (BEROSU) structure to a flexible part.
- 3) The portion between package body regio-oralis male screw Motobe of a flexible container and a bellows portion is the shape of dome state or conical shape.
- 4) It is disengageable to the cap with a nozzle, and a flexible package body at least before contents enclosure.
- 5) A nozzle equips 10 degrees of ascending vertical angles thru/or 90 degrees with the structure which crooked or curved from a container medial axis.
- 6) A nozzle tip can be opened for free passage with foam-connection gold of an endoscope forceps opening or the washing tube for nebulization and spraying.
- 7) It is covered with the coat pipe.

[0028]

One example of the gestalt of a flexible container is given to below, and it explains to it based on Drawings.

This flexible container comprises the flexible package body 1 which encloses a drug solution, and the cap 2 with a nozzle and the nozzle cap 3 which are fitted in or screwed on the body-ports part 101, as shown in drawing 1. The male screw 102 is formed in the periphery of the regio oralis, and it forms the fingerplate pressing part 103 in a pars basilaris ossis occipitalis, and the package body 1 has the bellows portion 105 and the label attachment part 106 for drug solution extrusion in the drum section 104, and the bellows portion 105 carries out a crush to it, and it is formed in it possible. The cap 2 with a nozzle has the male screw 203 on the periphery of the regio oralis (bung hole) of the female screw 202 which fits the fingerplate part 201 into the shoulder at the male screw 102 of the regio oralis of the package body 1 at the lower part, and a nozzle. Having the reinforcing rib 204 inside a cap shoulder with a nozzle, the nozzle cap 3 serves as the form where the female screw 301 screwed in the male screw 203 of the periphery of the regio oralis (bung hole) of a nozzle was formed.

[0029]

Drawing 2 is an example of the cap 2 with a nozzle shown in drawing 1, a fracture front view is shown in part and drawing 2 (a) shows the figure (half portion) which looked at drawing 2 (b) from the bottom side to the arrow direction. Drawing 2 is provided inside the cap 2 with a nozzle, and shows the reinforcing rib 204 which strengthens combination to the package body 1 of the cap 2 in contact with the shoulder of the upper part of the package body 1. The shape of the reinforcing rib 204 to provide is designed meet the outside of a package body, and the number of

ribs may be arbitrarily defined according to the construction material of a container etc., etc.  
[0030]

Drawing 3 is an example of the flexible package body 1 which encloses the drug solution shown in drawing 1. The male screw 102 is formed in the periphery of the package body regio oralis 101, the fingerplate pressing part 103 is formed in a pars basilaris ossis occipitalis, and it has the \*\*\*\*\* part 106 at the time of the drug solution extrusion which served both as the bellows portion 105 and label attachment part for drug solution extrusion, and the bellows portion 105 carries out a crush to the drum section 104, and is formed in it possible.

This flexible container comprises the flexible package body 1 which encloses a drug solution, and the cap 2 with a nozzle and the nozzle cap 3 which are fitted in or screwed on the body-ports part 101, as shown in drawing 4. The male screw 102 is formed in the periphery of the regio oralis, and it forms the fingerplate pressing part 103 in a pars basilaris ossis occipitalis, and the package body 1 has the bellows portion 105 for drug solution extrusion in the drum section 104, and the bellows portion 105 carries out a crush to it, and it is formed in it possible. The cap 2 with a nozzle has the male screw 203 on the periphery of the regio oralis (bung hole) of the female screw 202 which fits the fingerplate part 201 into the shoulder at the male screw 102 of the regio oralis of the package body 1 at the lower part, and a nozzle, It has the reinforcing rib 204 and the label attachment part 207 inside a cap shoulder with a nozzle, has the screw return prevention rib 206 in the female screw 202 lower part, and has the projection 205 which can recognize the nozzle bending direction at the time of use in the fingerplate part 201 (refer to drawing 4 (a)). The nozzle cap 3 serves as the form where the female screw 301 screwed in the male screw 203 of the periphery of the regio oralis (bung hole) of a nozzle was formed.

[0031]

Drawing 5 is an example of the cap 2 with a nozzle shown in drawing 4, a fracture front view is shown in part and drawing 5 (a) shows the figure (half portion) which looked at drawing 5 (b) from the bottom side to the arrow direction. Drawing 5 is provided inside the cap 2 with a nozzle, and shows the reinforcing rib 204 which strengthens combination to the package body 1 of the cap 2 in contact with the shoulder of the upper part of the package body 1. The shape of the reinforcing rib 204 to provide is designed meet the outside of a package body, and the number of ribs may be arbitrarily defined according to the construction material of a container etc., etc. It has the screw return prevention rib 206 in the female screw 202 lower part, and this rib 206 is formed in the four directions of 90 degree. The projection 205 which can recognize the nozzle bending direction at the time of use is formed in the fingerplate part 201.

Drawing 6 is an example of the flexible package body 1 shown in drawing 4. The male screw 102 is formed in the periphery of the package body regio oralis 101, the fingerplate pressing part 103 is formed in a pars basilaris ossis occipitalis, and it has the bellows portion 105 for drug solution extrusion, and the bellows portion 105 carries out a crush to the drum section 104, and is formed in it possible. It has the screw return prevention projection 107 in the lower part of the package body regio oralis 101.

[0032]

When using it, as shown in drawing 7 and drawing 8, the nozzle cap 3 of the flexible container A is removed, By carrying out press fitting of the nozzle tip of the cap 2 with a nozzle to the end connection (foam-connection gold or endoscope forceps opening) 41 of the washing tube (or endoscope) 4, and pressing to the fingerplate pressing part 103 of the pars basilaris ossis occipitalis of the package body 1, applying it, The bellows portion 105 is crushed and the drug solution in the package body 1 blows off in the washing tube 4.

In this example, as for the flexible package body 1, low density polyethylene, and the cap 2 with a nozzle and the nozzle cap 3 comprise polypropylene for each part, for example.

[0033]

A user replaces a flexible container with the method of crushing by a hand directly, and drawing 9 thru/or drawing 11 show how to perform using a use machine. In the following explanation, about a flexible container, identical codes are given to identical parts, and explanation is omitted.

Drawing 9 is an example using an injector and the catapult which has the same outside, and the

catapult 5 consists of the press bar 52 inserted into the cylinder-like main part 51 of a catapult, and the main part 51 of a catapult. Although the catapult 5 is made with transparent colorlessness or colored plastics, such as polystyrene and polypropylene, in respect of that the flexible container A inserted into the main part 51 of a catapult usually appears from the outside, and a weight saving, it is good also as metal.

[0034]

The main part 51 of a catapult had the size hole 53 which the nozzle at the tip of the flexible container A may expose at a tip, and is provided with the loading slot 54 for inserting the press bar 52 in the back end. In order to receive the main part of a catapult workability, it is good to form the fingerplate board 55. In drawing 9, although provided in the position of the loading slot 54 of the main part back end of a catapult, it is not limited to this position. Although the flexible container A is inserted from the loading slot 54 of the main part 51 of a catapult, a loading slot is established in the suitable part of the length direction of the main part 51 of a catapult, and it may enable it to usually insert it in it. The flexible container inserted into the main part 51 of a catapult is pressed and compressed with a press bar, and a hemostat is made to eject.

[0035]

Drawing 10 ~ 11 are the examples using the press auxiliary machine which consists of a barrel which provided the guidance notch of the finger when pressing a flexible container in the side. When pressing a flexible container, the bellows portion of a container inclines depending on how to hang the finger to a container, or how to push, and there are press and a case where it is compressed.

This example shows the example using the press auxiliary machine 6 which consists of the funnel-like pars basilaris ossis occipitalis 64 which has the guidance notch 62 of a finger when pressing the flexible container A formed in the side of the erection cylindrical body part 61 in the length direction, and has the opening 63 for the nozzles of the flexible container A at the pars basilaris ossis occipitalis of the cylinder section 61. The opening of the upper part of the cylinder section 61 is carried out, it inserts the flexible container A from here, hangs a finger on the bottom (fingerplate pressing part 103) of the container A, and extrudes the contents of the container A by depressing a finger along with the guidance notch 62. Since in this example it is stabilized and a container can be pressurized and compressed, the nozzle of the container A can be lengthened.

[0036]

Although drawing 11 is shown in the form where each member of the press auxiliary machine 6 shown in drawing 10 was separated, the flexible container A usually supplies the package body 1, and tube 2b for nozzles and the nozzle 2a to a user as a form which should consider it as one and attached the nozzle cap 3. The press auxiliary machine 6 is a simple structure made from a plastic, and since it can be considered as a cheap thing, it supplies in the flexible container A and the separated form, and also both can also be supplied as a set.

Tube 2b for nozzles is good also as what has a curve specific as a hard or half-rigid product made from a plastic, and good also as a linear shape tube. It is good also as a soft tube.

In using the catapult 5 and the press auxiliary machine 6, Without using the flexible container A as a bottle shaped vessel with the bottom 103, since the flexible container A is compressible in the stable form, The filling port of contents can be provided in the pars basilaris ossis occipitalis of a flexible container, pouring restoration of the contents can be carried out into a container from this filling port, and a filling port can be used as the container of the form which heat seals and closes laminate films, such as a plastic sheet, aluminum foil/polyethylene. A plastic cap can also be given.

[0037]

As for the shape of a container, since it is desirable for the quantity for which contents should use the flexible container of this invention like a hemostat to flow out almost correctly, it is not preferred that contents are the shape which cannot remain between bellows or cannot fully extrude contents.

When drawing 12 is a flexible container for catering to the above-mentioned request, and makes three steps the number of the bellows 12 of the package body 1 and a nozzle is turned



downward (i.e., when the container A is made to do a handstand), it is made for the container internal surface 12b of the bellows by the side of a nozzle to turn into a gently-sloping curved surface through which it flows caudad. The partial fracture side view of the flexible container with which drawing 12 (A) carried out the side view of the package body 1, and (B) carried out the cap 2 with a nozzle to the package body 1 and with which it equipped is shown.

Drawing 13 constitutes each stage (each bellows) of the bellows 12 so that the head 11 of the package body 1 of the flexible container A may be enlarged, may be turned caudad and it may become small. By considering it as such shape, when the package body 1 is compressed, the bellows of a container bottom is converged in the head 1 of a container, and contents are fully extruded. The partial fracture side view of the flexible container with which drawing 13 (A) carried out the side view of the package body 1, and (B) carried out the cap 2 with a nozzle to the package body 1 and with which it equipped is shown.

[0038]

The desirable mode in the flexible container of this invention, As mentioned above, are open for free passage into the foam-connection gold of plastic liquid medicine container ratio \*\*, such as cylindrical shape and the shape of an ellipse, an endoscope forceps opening, or the washing tube for nebulization and spraying currently used widely by drugs, such as the conventional ophthalmic solutions, If a container bottom is pushed with the thumb, it has structure which a bellows portion is compressed by the pressure and an inner solution tends to extrude easily. By giving an ascending vertical angle to a nozzle and considering it as the shape of type of "\*\*", an inner solution can be more easily extruded from a nozzle tip because it becomes possible to make this invention container open for free passage / hold at a moderate angle (theta) at foam-connection gold of an endoscope forceps opening or a washing tube.

[0039]

Therefore, in this invention the most suitable medicinal composition for hemostasis, A flexible part is a product made from a plastic, and at least including bellows (BEROSU) structure to a flexible part before contents enclosure, It is disengageable to the cap with a nozzle, and a flexible package body, and a nozzle, Equip 10 degrees - 40 degrees with the angle of gradient (theta) from a container medial axis, and 10 degrees of ascending vertical angles thru/or the structure which crooked or curved preferably 90 degrees a nozzle tip, It is a medicinal composition for partial hemostasis characterized by the thing which was sealed hermetically in foam-connection gold of an endoscope forceps opening or the washing tube for nebulization and spraying, and the flexible container which can be open for free passage, and which contain thrombin as an active principle at least, and contains 40 to 55% (W/V) of glycerin during a drug solution presentation.

[0040]

since the flexible container of this invention is only provided with the flexible package body 1, the cap 2 with a nozzle, and the nozzle cap 3 as an indispensable component, its structure is very simple --- manufacture --- it is easy and a manufacturing cost can be reduced.

The plastic container meant and designed by this appearance is widely applicable to a medicinal composition, a diagnostic drug, etc. which use not only the agent for partial hemostasis but an endoscope, and are applied or sprinkled in the upper part or a lower digestive tract. It excels in the purpose of preventing the malpractice especially by intravenous injection etc.

[0041]

[Example]

[Working example 1]

After adding purified water to L-arginine 0.87g and 2.8 g of sodium chloride and dissolving in them, 1.2g of acetic acid is added. A proper quantity of sodium hydroxide is added to this, and pH is adjusted to 6.3. After doing concentrated glycerin 100g addition of at this solution, 18.2mL is added and a thrombin solution is mixed calmly. Purified water was added and the whole quantity was set to 200mL, after adjusting pH to 6.3 in the chloride or sodium hydroxide of 0.1 mol/L. After filtrating this prepared solution aseptically with a membrane filter, 5 mL was poured distributively to each plastic container shown in drawing 1, and it sealed hermetically in it.

[Working example 2]

After adding purified water to L-arginine 0.87g and 2.8 g of sodium chloride and dissolving in



them, 1.2g of acetic acid is added. A proper quantity of sodium hydroxide is added to this, and pH is adjusted to 6.3. After doing concentrated glycerin 100g addition of at this solution, 18.2mL is added and a thrombin solution is mixed calmly. Purified water was added and the whole quantity was set to 200mL, after adjusting pH to 6.3 in the chloride or sodium hydroxide of 0.1 mol/L. After filtrating this prepared solution aseptically with a membrane filter, 5 mL was poured distributively to each plastic container shown in drawing 4, and it sealed hermetically in it.

[0042]

[The example 1 of contrast]

After adding purified water to L-arginine 0.87g and 2.8 g of sodium chloride and dissolving in them, 1.2g of acetic acid is added. A proper quantity of sodium hydroxide is added to this, and pH is adjusted to 6.3. After doing concentrated glycerin 100g addition of at this solution, 18.2mL is added and a thrombin solution is mixed calmly. Purified water was added and the whole quantity was set to 200mL, after adjusting pH to 6.3 in the chloride or sodium hydroxide of 0.1 mol/L. After filtrating this prepared solution aseptically with a membrane filter, it filled up the glass vials of content volume 20mL with 5 mL at a time, and the sealing plug was carried out with the rubber stopper and the aluminium cap.

[0043]

[The example 1 of an experiment]

When using both per working example 1 and example 1 of contrast, I got ten persons' panelist to check about a possibility of mistaking as injections. The experiment supposing actually sprinkling a drug solution under an endoscope was conducted, and the simple nature of use was evaluated. A test result is shown in Table 1. It has checked, when any panelist showed recognition that it was a different thing from injections and malpractice prevention had an effect.

[0044]

[Table 1]

表1 トロンビン液剤と注射剤との識別性試験結果

パネラー 番号	注射剤と誤認されにくいと感じたか否か		使用が簡便であると感じたか否か	
	プラスチック 容器	バイアル容器	プラスチック 容器	バイアル容器
1	○	×	○	×
2	○	×	○	×
3	○	×	○	×
4	○	×	○	×
5	○	×	○	×
6	○	×	○	×
7	○	×	○	×
8	○	×	○	×
9	○	×	○	×
10	○	×	○	×

[0045]

[The example 2 of an experiment]

The amount of residual liquid in the flexible container at the time of it being open for free passage into foam-connection gold of the washing tube for an endoscope forceps opening, and nebulization and spraying, and extruding a drug solution about working example 1, was examined by five persons' panelist.

A test result is shown in Table 2. Which panelist's amounts of residual liquid were very as few as several percent.

[0046]

[Table 2]

表2 トロンビン液剤の残留液量

パネラー番号	5 mL トロンビン液剤	
	内視鏡	洗浄チューブ
1	0.4 mL	0.35 mL
2	0.35 mL	0.4 mL
3	0.45 mL	0.4 mL
4	0.3 mL	0.45 mL
5	0.5 mL	0.4 mL
平均	0.4 mL	0.4 mL

[0047]

[Effect of the Invention]

As for this invention, a glass syringe or an injectable solution vessel provides the medicinal composition for partial hemostasis sealed hermetically in the clearly discriminable flexible container. Since the medicinal composition of this invention is intentionally removed in the process of using a glass syringe in process of administration operation, shortening of complicated operation in a medical site, prevention of contamination, prevention from product tampering, and fundamental prevention of a malpractice that tends to take place to the drugs for the oral administration local administration containing a vial bottle conventionally can be aimed at. choosing suitably the still more suitable plastic material about the whole container — structure — it is made simple, product cost is cheap, and since disposal can be given as it is, without moreover classifying after-use each part, facilitating also of the abandonment of infectious medical waste is carried out.

[Brief Description of the Drawings]

[Drawing 1] an example of the flexible container of this invention is shown — it is a fracture front view in part.

[Drawing 2] an example of the cap with a nozzle of the flexible container of this invention is shown — it is a deficit bottom view figure (b) in part with a fracture front view (a).

[Drawing 3] It is a package body (drug solution seat part) of the flexible container (drawing 1) of this invention.

[Drawing 4]an example of the flexible container of this invention is shown -- it is a fracture front view in part.

[Drawing 5]an example of the cap with a nozzle of the flexible container of this invention is shown -- it is a deficit bottom view figure (b) in part with a fracture front view (a). The perspective view of drawing 5 (b) is shown in a figure (c).

[Drawing 6]It is a package body (drug solution seat part) of the flexible container (drawing 4) of this invention (figure (a)). The perspective view of a figure (a) is shown in a figure (b).

[Drawing 7]It is a perspective view (the flexible container is open for free passage into foam-connection gold of the washing tube for nebulization and spraying.) showing the state of use of a flexible container.

[Drawing 8]It is a perspective view showing the situation where opened the flexible container for free passage directly to the endoscope forceps opening, and the drug solution is extruded.

[Drawing 9]It is a perspective view showing the catapult loaded with a flexible container.

[Drawing 10]It is a perspective view showing the example of use of a press auxiliary machine.

[Drawing 11]It is an exploded perspective view of the press auxiliary machine of drawing 10.

[Drawing 12]It is a perspective view showing other working example of a flexible container.

[Drawing 13]It is a perspective view showing other working example of a flexible container.

[Description of Notations]

1 A flexible package body (drug solution seat part)

101 package-body regio oralis

102 package-body regio-oralis male screw

103 fingerplate pressing part

104 package-body drum section

105 bellows portions

106 label attachment parts

107 screw return prevention projection

2 The cap with a nozzle

201 fingerplate parts

202 female screws

203 nozzle-mouth outside circumference male screw

204 reinforcing ribs

205 projections

206 screw return prevention rib

207 label attachment parts

3 Nozzle cap

301 nozzle-cap female screw

4 Washing tube

41 A liquid transport cap or an endoscope forceps opening

5 Catapult

6 Press auxiliary machine

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[Translation done.]

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203 nozzle-mouth outside circumference male screw

204 reinforcing ribs

205 projections

206 screw return prevention rib

207 label attachment parts

3 Nozzle cap  
301 nozzle-cap female screw  
4 Washing tube  
41 A liquid transport cap or an endoscope forceps opening  
5 Catapult  
6 Press auxiliary machine

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[Translation done.]



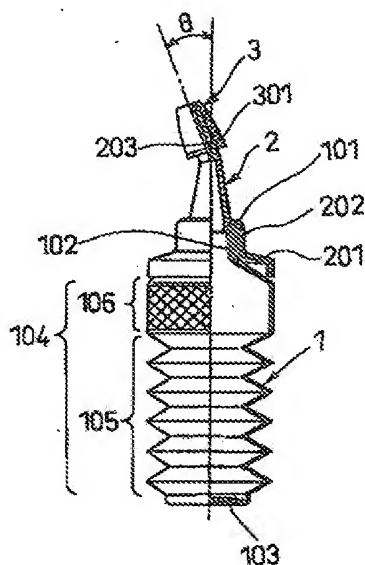
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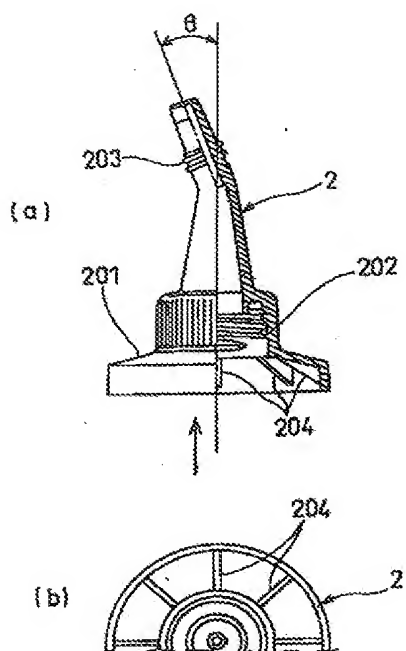
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## DRAWINGS

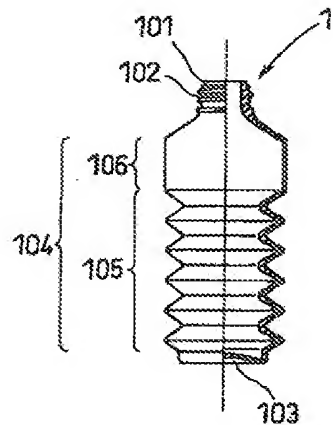
[Drawing 1]



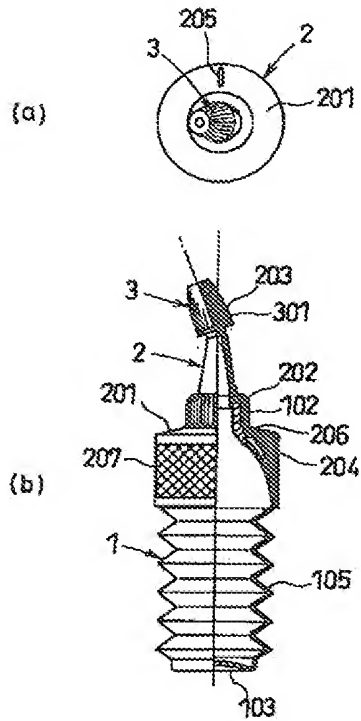
[Drawing 2]



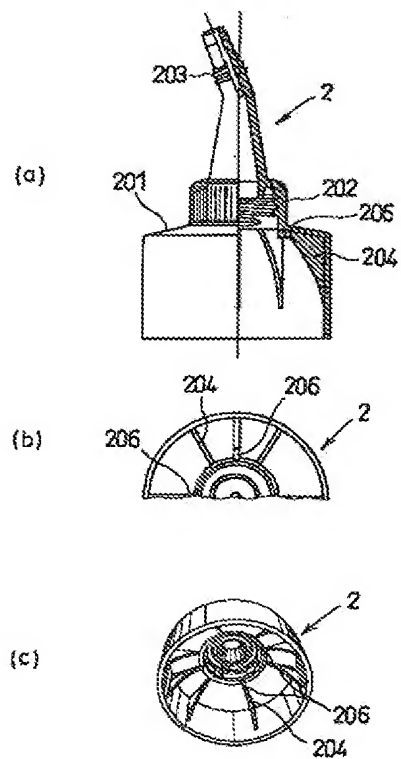
[Drawing 3]



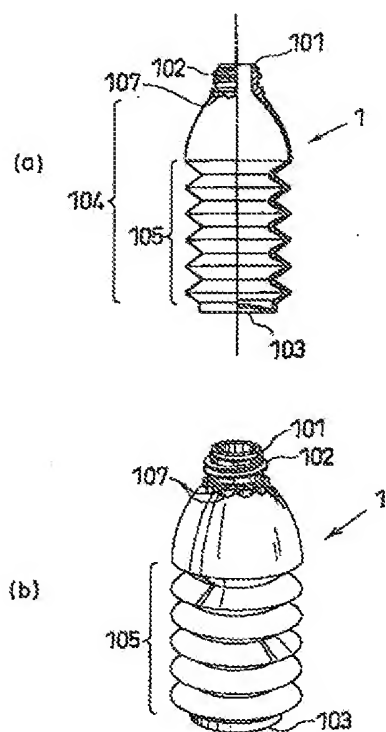
[Drawing 4]



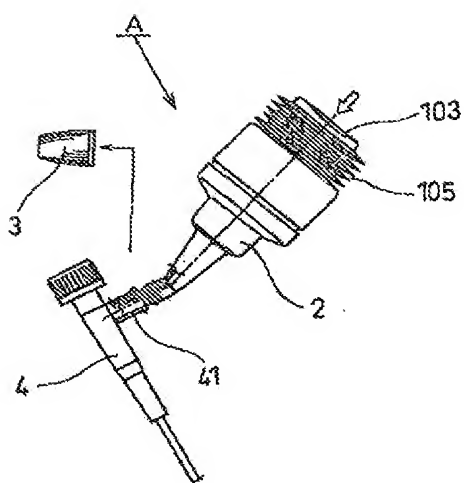
[Drawing 5]



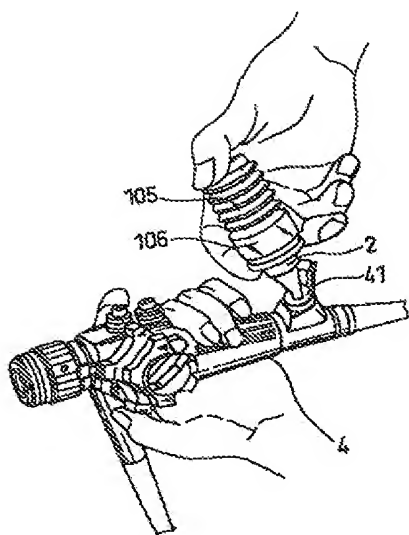
[Drawing 6]



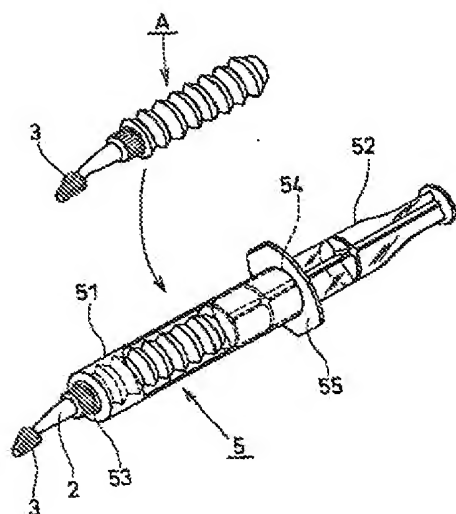
[Drawing 7]



[Drawing 8]

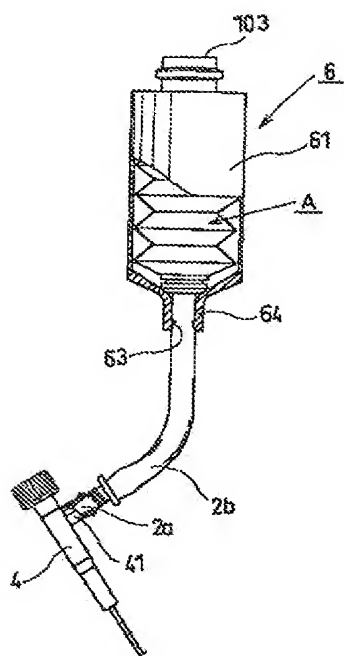


[Drawing 9]

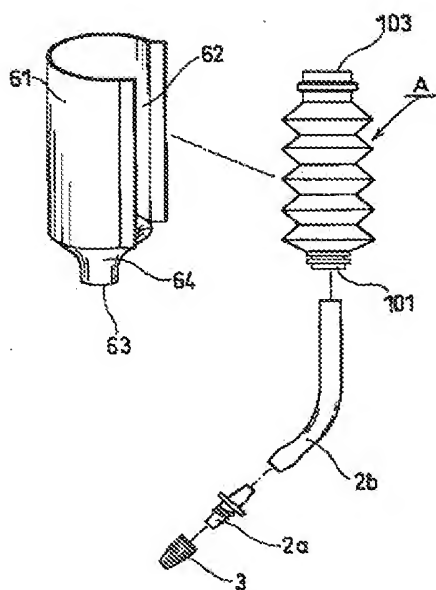


[Drawing 10]

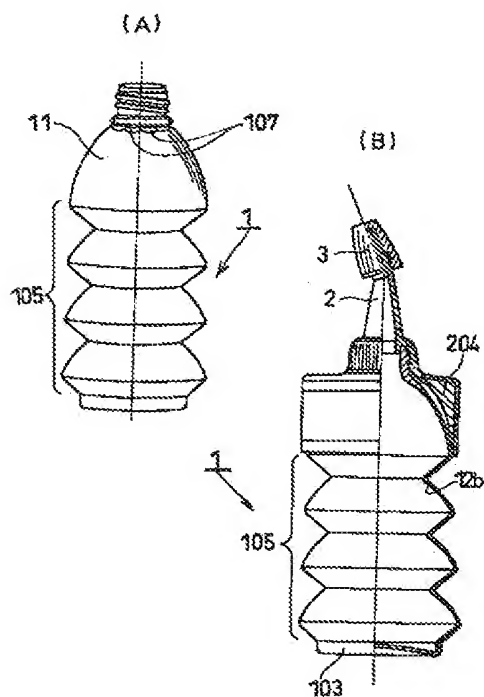




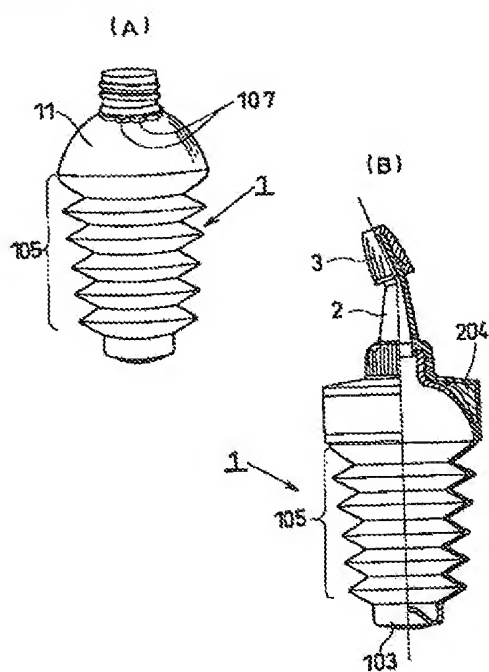
[Drawing 11]



[Drawing 12]



[Drawing 13]



[Translation done.]